REMARKS

Applicants are appreciative of the courtesies extended by Examiner Ly in an interview held in the U.S. Patent and Trademark Office on December 3, 2002. Applicants discussed the Hoe and Kobayashi references and proposed amendments to the claims. Applicants note that the following remarks generally track the substance of the interview.

In the final Office Action dated August 13, 2003, all of the pending claims were rejected. Pending claims 15-20 were rejected under 35 U.S.C. § 112, first paragraph. Pending claims 1, 3-5, 7, 8, 10-14, 21-36, and 38-41 were rejected under 35 U.S.C. § 112, second paragraph. Pending claims 1, 3-5, 12-14, 21, 25-30, 32-34, 36, 39-41 were rejected under 35 U.S.C. § 102(b) as being anticipated by Hoe et al. Pending claims 1, 3-5, 7, 8, 10-14, 21-36, and 38-41 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hoe in combination with Frenay et al. taken with O'Brien et al. in view of Paradiso et al. (U.S. Patent No. 6,404,340).

By this amendment, Applicants have amended claims 1, 8, 16-17, 21-23, 27-28, 30 and 32-34. Applicants have also added new claims 42 through 44. Claims 15, 18-20, 37 and 39-41 are canceled. Support for these amendments can be found at least, for example, at page 21, lines 11-24 (the first region comprising a variable number of tandem repeats); page 14, lines 1-5 and page 24, lines 9-10 (storing DNA sequence data in the database); page 25, line 15 (storing a physical location of a patient or object in the database); page 25, lines 14-23 (tracking the spread of the infection based on the physical locations stored in the database); page 27, line 15 - page 28, line 2 (providing a warning based on the tracking of the spread of the bacteria wherein the warning allows the recipient of the information to control the further spread of the bacterial infection). Applicants respectfully request favorable reconsideration of this application.

Rejections Under 35 U.S.C. § 112

The Examiner rejected claims 15-20 under 35 U.S.C. § 112, first paragraph. Claims 15 and 18-20 are canceled. Claims 16 and 17 have been amended for clarification to address the Examiner's concerns. The Examiner rejected claims 1, 3-5, 7, 8, 10-14, 21-36, and 38-41 under 35 U.S.C. § 112, second paragraph. The Applicant has amended claims 1, 39 and 40 for clarification.

Rejection Under 35 U.S.C. § 102

The Examiner rejected claims 1, 3-5, 12-14, 21, 25-30, 32-34, 36, and 39-41 under 35 U.S.C. § 102(b) as being anticipated by Hoe.

Hoe discloses obtaining 100 group A *streptococcus* (GAS) isolates from patients in Texas ("the Texas isolates") and sequencing part of the *emm* gene from each isolate. (p. 255) Hoe discloses comparing the sequence data from the 100 Texas isolates to sequence data in an *emm* database to differentiate the 100 Texas isolates; however, Hoe does not disclose that the sequence data from any of the analyzed 100 Texas isolates is stored in a database. Hoe discloses that the database contains *emm* sequence data for organisms from "global sources" (*i.e.*, organisms obtained from around the world) (p. 255, col. 2). Hoe does not disclose that the global database stores the physical locations from where the organisms where obtained.

Hoe further discloses sequencing the *sic* gene in 30 of the 100 Texas isolates which were identified as M1 serotype ("the 30 M1 Texas isolates"). Hoe discloses that the sequence data for the 30 M1 Texas isolates is compared to sequence data in a *sic* database of 1200 M1 isolates obtained from "worldwide sources." (p. 256, col. 1). Again, Hoe does not disclose that the sequence data for the analyzed 30 M1 Texas isolates is stored in a database. Hoe also does not disclose that the *sic* worldwide database stores any physical locations from where the organisms were obtained.

Lastly, Hoe discloses that the Direct Repeat (DR) region of the 30 M1 Texas isolates was analyzed to determine the variability of the DR region among the 30 M1 Texas isolates. Hoe does not disclose that the sequence data from the DR region for the 30 M1 Texas isolates was compared to sequence data in a database (although an M1 GAS database at the University of Oklahoma was used to identify a region of the GAS chromosome that contained DR elements). (p.259-260). Hoe's study concludes that sequencing the *sic* gene was the most effective for differentiating among M1 isolates. (p. 261, column 1).

In summary, Hoe discloses a study of 100 GAS Texas isolates, 30 of which were M1 isolates. Hoe does not disclose that any of the sequence data from the analyzed Texas isolates was stored in a database. Hoe also does not disclose storing locations of patients or objects from which any isolates were obtained in a database.

Hoe does not anticipate or suggest amended claim 1 for several reasons. First, Hoe does not disclose storing in a database a physical location of a patient or object for each of a plurality of bacterium samples. Second, Hoe does not disclose comparing the sequence data stored in the database of at least two of a plurality of bacterium samples. Hoe only discloses comparing the sequence data from the Texas isolates (not stored in a database) to sequence data in the *emm* and *sic* databases. Third, Hoe does not disclose tracking the spread of the bacteria based on the physical locations of identified patients or objects stored in the database. Fourth, Hoe does not disclose sequencing a region of DNA comprising a variable number of tandem repeats (VNTRs). Fifth, Hoe does not disclose providing a warning based on the tracking of the spread of the bacteria wherein the warning allows the recipient of the warning to control the further spread of the bacterial infection. Hoe therefore neither anticipates nor suggests claim 1. The other independent and dependent claims are also neither anticipated nor suggested by Hoe for similar reasons.

The features recited in claim 1 allow the system of the present invention to provide a continuous and automated monitoring of hospitals and other facilities. The claimed features thus allow the system of the present invention to provide a rapid response to an incipient outbreak condition so that appropriate infection control measures can be taken before the outbreak becomes a serious problem.

Rejections Under 35 U.S.C. § 103(a)

Pending claims 1, 3-5, 7, 8, 10-14, 21-36, and 38-41 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hoe in combination with Frenay et al. taken with O'Brien et al. in view of Paradiso et al. (U.S. Patent No. 6,404,340).

Frenay and Kobayashi (submitted in a supplemental IDS) both disclose the results of studies analyzing the effectiveness of sequencing the polymorphic X-region of the protein A gene (*spa*) of methicillin-resistant Staphylococcusus aureus (MRSA) strains for use as a molecular typing tool. None of Hoe, Frenay or Kobayashi disclose the storing the physical locations of patients or objects in a database, as recited in claim 1. None of these references disclose tracking the spread of bacteria utilizing physical locations of identified patients or objects stored in the database. None of these references disclose providing a warning based on the tracking of the spread of the bacteria wherein the warning allows the recipient of the information to control the further spread of the bacteria. The claimed invention is thus patentable over Hoe in combination with Frenay or Kobayashi.

O'Brien reports the results of a study which tests the hypothesis that individuals chronically non-compliant with antituberculosis chemotherapy are vectors for ongoing transmission of the disease in the community. O'Brien discloses the use a standardized IS6110-based Southern blot hybridization protocol to genotype *M Tuberculosis* isolates recovered from patients confined in a detention unit of a hospital. O'Brien also discloses a

"linked database of fingerprints from isolates around the United States would . . . likely enhance tuberculosis control." (page 391, column 1, lines 38-40).

O'Brien does not disclose sequencing a region of the DNA (the RFLP DNA fingerprint analysis compares lengths of strands of DNA, but does not involve sequencing the DNA). O'Brien also does not disclose storing in a database sequence data and physical locations of patients or objects. O'Brien also does not disclose tracking the spread of a bacterial infection utilizing physical locations of identified patients or objects stored in the database. O'Brien also does not disclose providing a warning based on the tracking of the spread of the bacteria wherein the warning allows the recipient of the information to control the further spread of the bacterial infection.

Paradiso discloses tracking the position of magnetically coupled resonant structures. Paradiso also discloses attaching a tag to a tumor during a medical procedure to irradiate the tumor; the tag is used to monitor the location of the tumor as a patient breathes or otherwise moves. (See Col. 2, lines 37-47.) Paradiso is not analogous to the system of the present invention, which is a system for tracking the spread of bacteria. Paradiso does not disclose storing sequence data and physical locations of patients or objects in a database. Paradiso also does not disclose tracking the spread of a bacterial infection utilizing physical locations of identified patients or objects stored in a database. Paradiso also does not disclose providing bacterial spread information based on the tracking of the spread of the bacterial infection wherein the bacterial spread information allows the recipient of the information to control the further spread of the bacterial infection.

de Lancastre (submitted in a supplemental IDS) discloses the use of pulsed-field gel electrophoresis (PFGE) analysis of bacterial DNA for use in a tracking system to assist hospitals, clinics, and chronic care facilities in controlling the spread of multidrug-resistant pathogens. PFGE does not involve sequencing the DNA. As described in the background

section of the present application, PFGE analysis has a number of problems that the present invention overcomes. Specifically, comparing PFGE patterns is subjective and does not always differentiate different strains of bacteria. PFGE is also laborious and time-consuming and the images are the difficult to store in a database because they take up too much memory. (See Background of Application, pages 5-6). de Lancastre does not disclose sequencing DNA and storing the sequence data in a database with the physical locations of patients or objects. de Lancastre also does not disclose comparing DNA sequence data, and determining the phylogenetic relatedness of bacteria based on differences between sequence data. de Lancastre also does not disclose tracking the spread of a bacterial infection utilizing physical locations of identified patients or objects stored in the database.

None of the above references therefore anticipate or suggest the claimed invention.

New Claims 42-44

New claims 42 through 44 are allowable for at least the reason given above. New claim 42 is further allowable because none of the cited references disclose determining the phylogenetic relatedness of the sequence data between the compared samples based on: a) the number of insertions and deletions of individual nucleotides; and b) the number of insertions and deletions of repeat cassettes, wherein a repeat cassette comprises a sequence of nucleotides which repeats in the first region of the deoxyribonucleic acid.

New claim 43 is further allowable because none of the cited references disclose determining the phylogenetic relatedness of the sequence data between the compared samples, wherein the insertion or deletion of a repeat cassette is treated as a single genetic event, wherein a repeat cassette comprises a sequence of nucleotides which repeats in the first region.

New claim 44 is further allowable because none of the cited references disclose

transmitting the sequence data to the server over a computer network prior to storing the sequence data in a database.

CONCLUSION

In conclusion, Applicants submit that this case is in condition for allowance and respectfully request favorable reconsideration of this case.

The Commissioner is authorized to charge insufficient fees and credit overpayment associated with this communication to Deposit Account No. 19-5127, order # 19124.0002.

Respectfully submitted,
SWIDLER BERLIN SHEREFF FRIEDMAN, LLP

Dated: February 11 , 2003

By:  Reg. No. 47,252
For Edward A. Pennington, Registration No. 32,588
SWIDLER BERLIN SHEREFF FRIEDMAN, LLP
3000 K Street, NW, Suite 300
Washington, D.C. 20007
(202) 424-7756 Telephone
(202) 295-8478 Facsimile